REMARKS

Claims 61-115 are pending. Claims 67, 69, 70, 74, 76, 78, 80, 81, 83, 85, 87, 95-97, 101, 103, 105, 107, 108, 110, 112, and 114 are under examination. Claim 95 has been amended to correct a typographical error. Accordingly, this amendment does not raise an issue of new matter and entry thereof is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 69, 78, 96 and 105 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed. Applicants respectfully submit that the claims are clear and definite. In the Office Action, the term "PS341" is indicated to be unclear. Applicants respectfully submit that the term "PS341" is well known to those skilled in the art (see Exhibit 1, printout from website of Multiple Myeloma Research Foundation). As taught in the specification on page 20, lines 23-26, PS341 is an exemplary anti-cancer agent that can be used in combination with paricalcitol (see page 21, lines 3-5). Thus, Applicants respectfully submit that the term "PS341" is clear to one skilled in the art and that claims reciting the term "PS341" are clear and definite. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

The rejection of claims 67, 69, 83, 85, 95, 96, 110 and 112 under 35 U.S.C. § 103 as allegedly obvious over Blanchard et al., WO 02/30430, in view of Sung et al., U.S. Patent No. 6,624,138, and in further view of ElGenidi, Eur. J. Cancer 37, supplement 6, p. S357 (abstract), is respectfully traversed. Applicants respectfully submit that the claimed methods are unobvious over Blanchard et al., alone or in combination with Sung et al. and/or ElGenidi.

Claim 67 is directed to a method of reducing the severity of a proliferative disorder by administering to an individual having the proliferative disorder, wherein the proliferative disorder is selected from myelodysplastic syndrome, leukemia, acute myelocytic leukemia, acute lymphocytic leukemia, multiple myeloma, breast cancer, colon cancer and prostate cancer, an effective amount of paricalcitol and an anti-cancer agent, wherein the combination of paricalcitol and the anti-cancer agent reduces cell proliferation. Claim 95 is directed to a method of reducing

cancer recurrence, comprising administering to an individual in cancer remission, wherein the cancer in remission is selected from myelodysplastic syndrome, leukemia, acute myelocytic leukemia, acute lymphocytic leukemia, multiple myeloma, breast cancer, colon cancer and prostate cancer, an effective amount of paricalcitol and an anti-cancer agent, wherein the combination of paricalcitol and the anti-cancer agent reduces cancer cell proliferation.

Applicants respectfully submit that Blanchard et al. does not teach or suggest the claimed methods. At best, Blanchard et al. describes the use of vitamin D_2 compounds for reducing, preventing or treating hair loss (alopecia) induced by a chemotherapeutic agent. However, Blanchard et al. provides no teaching or suggestion of the claimed methods of reducing the severity of a proliferative disorder or reducing cancer recurrence. Furthermore, as acknowledged in the Office Action on page 4, ElGenidi merely corroborates that alopecia is a side effect of chemotherapy, and in fact describes the use of a digital scalp cooling system for the prevention of chemotherapy-induced alopecia. Moreover, Sung et al. describes solidifiable drug-containing biological material and huge laundry list of numerous exemplary drugs suitable for inclusion in the material, including analgesics, antibiotics, antidepressants, etc. However, Sung et al. provides no teaching or suggestion of using paricalcitol to reduce the severity of a proliferative disorder or reduce cancer recurrence, as in the claimed methods.

To establish a *prima facie* case, the Office must satisfy three requirements. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. See *Karsten Mfg. Corp. v. Cleveland Gulf Co.*, 242 F.3d 1376, 1385, 58 U.S.P.Q.2d 1286, 1293 (Fed. Cir. 2001); *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1352, 48 U.S.P.Q.2d 1225, 1232 (Fed. Cir. 1998); *Northern Telecom v. Datapoint Corp.*, 908 F.2d 931, 934, 15 U.S.P.Q.2d 1321, 1323 (Fed. Cir. 1990). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. In other words, a hindsight analysis is not allowed. See *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991); *In re Erlich*, 3 U.S.P.Q.2d 1011, 1016 (Bd. Pat. App. & Int. 1986). Lastly, the prior art reference or combination of

references must teach or suggest all the limitations of the claims. See *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

As the Supreme Court recently stated in *KSR v. Teleflex*, 550 U.S. (2007):

> When it first established the requirement of demonstrating a teaching, suggestion or motivation to combine known elements in order to show that the combination is obvious, the Court of Customs and Patent Appeals captured a helpful insight. [citation omitted] As is clear from cases such as Adams, a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Applicants respectfully maintain that the Office has not met the burden the law allocates to it with regard to establishing a *prima facie* case of obviousness, which requires that the prior art references relied upon give rise to the requisite motivation to combine their content and, when viewed in combination, provide the skilled person with a reasonable expectation of success to achieve the claimed invention. Applicants respectfully submit that a *prima facie* case of obviousness has not been established, and therefore the claimed methods are unobvious over Blanchard et al., alone or in combination with Sung et al. and/or ElGenidi. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 67, 69, 70, 76, 80, 81, 87, 95-97, 103, 107, 108 and 114 under 35 U.S.C. § 103 as allegedly obvious over Blanchard et al., *supra*, in view of Tidmarsh et al., U.S. Patent No. 7,001,888, in further view of Sung et al., *supra*, and further in view of ElGenidi, *supra*, is respectfully traversed. Applicants respectfully submit that the claimed methods are unobvious over Blanchard et al., alone or in combination with Tidmarsh et al. and/or Sung et al. and/or ElGenidi.

As discussed above, none of Blanchard et al. and/or Sung et al. and/or ElGenidi teaches or suggests Applicants' claimed methods. Moreover, Applicants respectfully submit that Tidmarsh et al. does not cure the deficiencies of Blanchard et al. and/or Sung et al. and/or

ElGenidi. At best, Tidmarsh et al. describes compounds for treating cancer. However, Applicants respectfully submit that the claimed methods of reducing the severity of a proliferative disorder and reducing cancer recurrence are neither taught nor suggested in any of Blanchard et al., Sung et al., ElGenidi or Tidmarsh et al., alone or in combination. For the reasons discussed above, Applicants respectfully submit that a *prima facie* case of obviousness has not been established, and therefore the claimed methods are unobvious over Blanchard et al., alone or in combination with Sung et al. and/or ElGenidi and/or Tidmarsh et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 67, 69, 74, 78, 95, 96, 101 and 105 under 35 U.S.C. § 103 as allegedly obvious over Blanchard et al., *supra*, in view of Shashoua et al., U.S. Patent No. 5,795,909, in further view of Sung et al., *supra*, and further in view of ElGenidi, *supra*, is respectfully traversed. Applicants respectfully submit that the claimed methods are unobvious over Blanchard et al., alone or in combination with Shashoua et al. and/or Sung et al. and/or ElGenidi.

As discussed above, none of Blanchard et al. and/or Sung et al. and/or ElGenidi teaches or suggests Applicants' claimed methods. Moreover, Applicants respectfully submit that Shashoua et al. does not cure the deficiencies of Blanchard et al. and/or Sung et al. and/or ElGenidi. At best, Shashoua et al. describes conjugates of cis-docosohexaenoic acid and taxanes for treating proliferative disorders. However, Applicants respectfully submit that the claimed methods of reducing the severity of a proliferative disorder and reducing cancer recurrence are neither taught nor suggested in any of Blanchard et al., Sung et al., ElGenidi or Shashoua et al., alone or in combination. For the reasons discussed above, Applicants respectfully submit that a *prima facie* case of obviousness has not been established, and therefore the claimed methods are unobvious over Blanchard et al., alone or in combination with Sung et al. and/or ElGenidi and/or Shishoua et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP

/Deborah L. Cadena/

Deborah L. Cadena
Registration No. 44,048

4370 La Jolla Village Drive, Suite 700
San Diego, CA 92122
Phone: 858.535.9001 DLC:llf
Facsimile: 858.597.1585
Date: August 27, 2007

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Home > Treatments > Velcade® (bortezomib)

IMPORTANT MESSAGE:
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myeloma research.

Velcade® (bortezomib)

Full Name:	Velcade® (bortezomib) for Injection
Other Names:	PS-341, MLN341, and LDP-341
Description:	Proteasome inhibitor (intravenous)
Phase:	Approved in over 40 countries worldwide, including the I
Company:	Millennium Pharmaceuticals, Inc. www.millennium.com www.velcade.com

What It Is

Velcade is the first in a class of medicines called proteasome inhibitors ar treatment in more than a decade to be approved for patients with multip 2003. It received full approval for use in patients who have received one 2005.

Based on promising Phase II data in the front-line setting, Millennium ha several large Phase III trials exploring Velcade-based regimens in this pa population. Velcade is also under investigation in other hematologic canc certain types of lymphoma, and in a variety of solid cancers, including pr breast, and ovarian cancer.

How It Works

Overview

Velcade is a potent, specific, and reversible proteasome inhibitor and the this type to enter clinical trials. Proteasomes are present in all cells and f regulate cell growth. In nonclinical studies, normal cells appear to be abl from intermittent proteasome inhibition, but many types of cancer cells u apoptosis (programmed cell death) when proteasomes are inhibited, eve time.

Details on Velcade's Mechanism of Action

The proteasome is an enzyme complex that exists in all cells and plays a role in degrading proteins involved in the cell cycle, growth of new blood (angiogenesis), cell adhesion, cytokine production, apoptosis, and other cellular processes. Many of the processes that rely on proteasome functi contribute to the growth and survival of cancer cells. Velcade is a potent inhibitor of the proteasome. By disrupting normal cellular processes, prot inhibition promotes apoptosis. Non-clinical data has demonstrated that c more susceptible to the effects of proteasome inhibition than normal cell reversibility of proteasome inhibition with Velcade, normal cells can reco effects, whereas cancer cells are more likely to undergo apoptosis.

Click here to go to the Millennium Pharmaceuticals, Inc. Web site to view that shows how proteasome inhibitors work.